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Original Article

Determination of the Relationship between Red Cell Distribution Width, NT-proBNP, and cTnT in Acute Myocardial Infarction Patients

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Abstract

Background: Acute myocardial infarction (AMI) is the major cause of death worldwide; thus, the requirement for early diagnosis is becoming increasingly important to allow initiation of lifestyle changes or appropriate medical intervention.

Aim: This study aims to investigate the relationship of several parameters of complete blood count (CBC) including RDW with N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiac troponin T (cTnT) in a cohort of acute myocardial infarction (AMI) patients.

Methods: A total of 45 participants (30 patients diagnosed with AMI and 15 healthy individuals) at Sohag Cardiology and Gastroenterology Center, Department of Cardiology and CCU from 1st March to 30th September 2023. were screened for enrollment in this prospective study. All agreed to participate in this prospective study, then they were divided into 2 main groups: 1st case group (30 patients diagnosed with AMI) and 2nd control group(15 healthy individuals not known to have AMI), they all were subjected to routine investigation (CBC including RDW) and specific investigations (NT-proBNP and cTnT).

Results: This case-control study was conducted among 45 participants then they were divided into 2 main groups: 1st case group (30 patients diagnosed with AMI) and 2nd control group(15 healthy individuals not known to have AMI), To find that there is a positive relationship between Red Cell Distribution Width, NT-proBNP and cTnT in Acute Myocardial Infarction Patients.

Conclusion: High levels of RDW were associated with AMI at admission and RDW is a widely available marker with no additional costs, in contrast to other novel markers of cardiovascular risk.

A high RDW may be associated with the severity and instability of acute myocardial infarction.

The combined use of presentation values of cTnT and its absolute change in the following hours has a significantly higher diagnostic accuracy for AMI than relative changes and seems therefore to be the preferred criteria to

Keywords: Acute myocardial infarction, RDW, NT-proBNP, cTnT

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Introduction

Acute myocardial infarction is one of the leading causes of death in the developed world. The prevalence of the disease approaches three million people worldwide, with more than one million deaths in the United States annually. Acute myocardial infarction can be divided into two categories, non-ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI). Unstable angina is similar to NSTEMI. However, cardiac markers are not elevated. [1-3]

Red cell distribution width (RDW), is a measure of the variability in size of circulating erythrocytes,[4].is calculated by automated blood cell counters as part of the routine blood cell count analysis. Traditionally, RDW and mean corpuscular volume are used in the differential diagnosis of anemia, particularly anemias that are microcytic (caused by iron deficiency) or macrocytic (due to vitamin B_{12} or folate deficiency). An increased RDW can also result from conditions that modify the shape of red blood cells due to the premature release of immature cells into the bloodstream, hemoglobinopathies, or other hematological diseases.[5, 6]

The association between RDW and MI has previously been reported mainly in patients with known cardiovascular (CV) disease or heart failure. [7, 8] Although growing evidence supports the hypothesis that high RDW is associated with an unfavorable CV risk profile and higher total and CV mortality in various populations, the impact of RDW on the risk of incident MI in a general population is unclear. Consequently, we aimed to investigate whether RDW was associated with the risk of first-ever event of MI in a large prospective study with participants recruited from a general population. [9, 10]

Patients and methods

This is a Case-control study conducted at Sohag Cardiology and Gastroenterology Center, Department of Cardiology and CCU from 1st March to 30th September 2023. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Sohag University on 12/12/2022 under IBR registration number: **Soh-Med-22-12-07**. Written informed consent was obtained from all participants.

A total of 45 participants (30 patients diagnosed with AMI and 15 healthy individuals) at Sohag Cardiology and Gastroenterology Center, Department of Cardiology and CCU from 1st March to 30th September 2023. were screened for enrollment in this prospective study. All agreed to participate in this prospective study, then they were divided into 2 main groups: 1st case group (30 patients diagnosed with AMI) and 2nd control group(15 healthy individuals not known to have AMI), they all were subjected to routine investigation (CBC including RDW) and specific investigations (NT-proBNP and cTnT).

Statistical analysis:

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). The Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing an unpaired Student's t-test. Quantitative non-parametric data were presented as the median and interquartile range (IQR) and were analyzed by Mann Whitney test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. The area under the curve (AUC) evaluates the overall test performance. Multivariate regression was also used to estimate the relationship between a dependent variable and more independent variables. A two-tailed P value < 0.05 was considered statistically significant.

Results

The study was carried out at Sohag Cardiology and Gastroenterology Center among 30 cases of AMI and matched with 15 controls from 1st March to 30th September 2023. The mean age of the studied participants was (57.36 ± 10.8) years. 60% of the studied participants were males. RDW,

Cardiac troponin T, and NT-proBNP) were assessed among the studied participants.

Patient demographics and descriptive data:

A review of the data of the studied cases of AMI included detailed socio-demographic characteristics (age and gender) and results of RDW, cTnT, and NT-proBNP at the time of admission and discharge, as shown in Table (1).

Table 1 Socio-demographic characteristics of the studied participants.

			Cases (n = 30)	Controls (n = 15)	Total (n = 45)	P-value
Age (years)	**Mean ± SD**		59.2 ± 10.4	53.6 ± 11.1	57.36 ± 10.8	0.1 #
	Range		(40-80)	(32-70)	(32 – 80)	
Gender	**Male**	**No.**	19	8	27	0.5 **
		%	70.4	29.6	60	
	Female	**No.**	11	7		
		%	61.1	38.9	40	

P-value is calculated by Independent Samples T-test,

** P-value is calculated by Chi-square.

Furthermore, there was a statistically significant difference between the studied participants according to RDW, cTnT, and NT- proBNP (P-value <0.05), as shown in Table (2). Pairwise comparison indicated that there was a statistically significant difference between cases at discharge and controls according to RDW, cTnT, and NT-proBNP (P2 < 0.05). Also, there was a statistically significant difference between cases at admission and controls according to cTnT and NT-proBNP (P3 < 0.05). Cases at admission showed a significant increase in the percentage of RDW in comparison to the percentage of cases at discharge and control group (13.2 ± 1.5, 12.4 ± 1.1, and 12.1 ± 0.8) % respectively, as shown below in figure (1). As regards cTnT, cases at discharge showed a significant increase in comparison to cases at admission and control group (2572.6 ± 755.6, 1054.3 ± 1007.4 and 27.7 ± 6.6) (ng/mL) respectively, as shown below in figure (2). As regards NT-proBNP, cases at discharge showed a significant increase in comparison to cases at admission and control group (2301 ± 2199.2, 298.5 ± 321, and 44.6 ± 8.4) (pg/mL) respectively, as shown below in figure (3)

Table 2: Comparison between the studied participants in RDW, TNT, and NT- proBNP

		Cases (n=30)		Controls (n = 15)	P	P1	P2	P3
		At admission	At discharge					
RDW (%)	Mean ± SD	13.2 ± 1.5	12.4 ± 1.1	12.1 ± 0.8	0.03*	0.100*	0.06	1.0
	Median	13.2	12.2	12.0				
cTnT (ng/mL)	Mean ± SD	1054.3 ± 1158.4	2572.6 ± 755.6	27.7 ± 6.6	0.001*	1.0	0.001*	0.005*
	Median	526	2785	27				
NT-proBNP (pg/mL)	Mean ± SD	298.5 ± 321	2301 ± 2199.2	44.6 ± 8.4	0.001*	1.0	0.001*	0.002*
	Median	208	1589.5	44				

* Level of significance < 0.05, P-value is calculated by Kruskal–Wallis test, Adjusted P-value of pairwise comparison P1 cases at admission Vs cases at discharge, P2 Cases at discharge Vs controls, P3 cases at admission Vs controls.

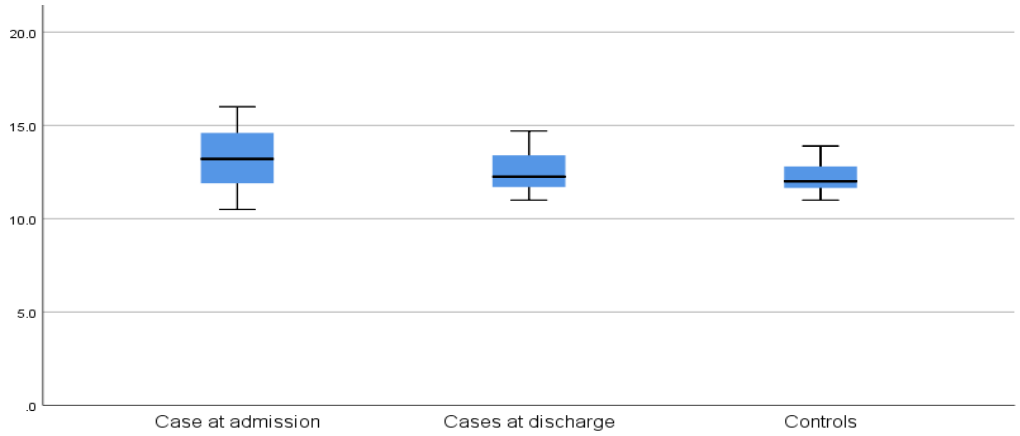

Figure 1: RDW comparison between the studied participants.

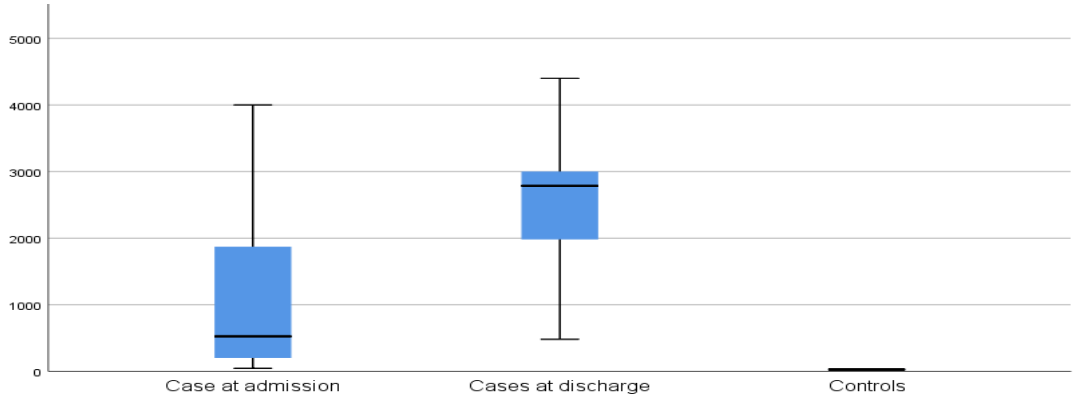

Figure 2: cTNT comparison between the studied participants.

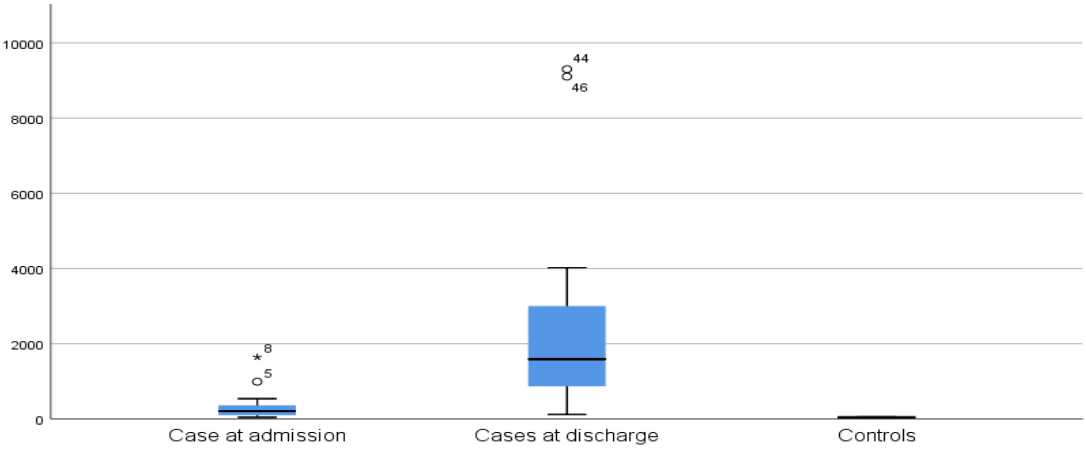

Figure 3: NT- proBNP comparison between the studied participants.

There was a statistically significant difference between cases either at admission or at discharge according to RDW, cTnT, and NT-proBNP (P-value < 0.05), as shown in Table (3). As regards RDW, the mean of RDW among cases at discharge shows a significant decrease in comparison to RDW at admission (12.4 ± 1.1 and 13.2 ± 1.5) respectively, as shown in Figure (4). However, cTnT of cases at the time of discharge shows a significant increase in comparison to that level at admission (2572.6 ± 755.6 and 1054.3 ± 1158.4) respectively, as illustrated in figure (5). Also, NT-proBNP shows a significant increase at discharge in comparison to that level at admission (2301 ± 2199.2 and 298.5 ± 321), as described below in Figure (6).

Table 3: Comparison between AMI cases in RDW, cTNT, and NT- proBNB.

		Cases at admission (n=30)	Cases at discharge (n=30)	P-value ^
RDW (%)	**Mean ± SD**	13.2 ± 1.5	12.4 ± 1.1	< 0.001*
	Median	13.2	12.2	
	Range	(10.5 – 16)	(11 – 14.7)	
cTnT (ng/mL)	**Mean ± SD**	1054.3 ± 1158.4	2572.6 ± 755.6	< 0.001*
	Median	526	2785	
	Range	(45-4000)	(483-4400)	
NT-proBNP (pg/mL)	**Mean ± SD**	298.5 ± 321	2301 ± 2199.2	< 0.001*
	Median	208	1589.5	
	Range	(45 – 1643)	(1 – 9298)	

* Level of significance < 0.05, ^ P-value is calculated by Wilcoxon signed-rank test.

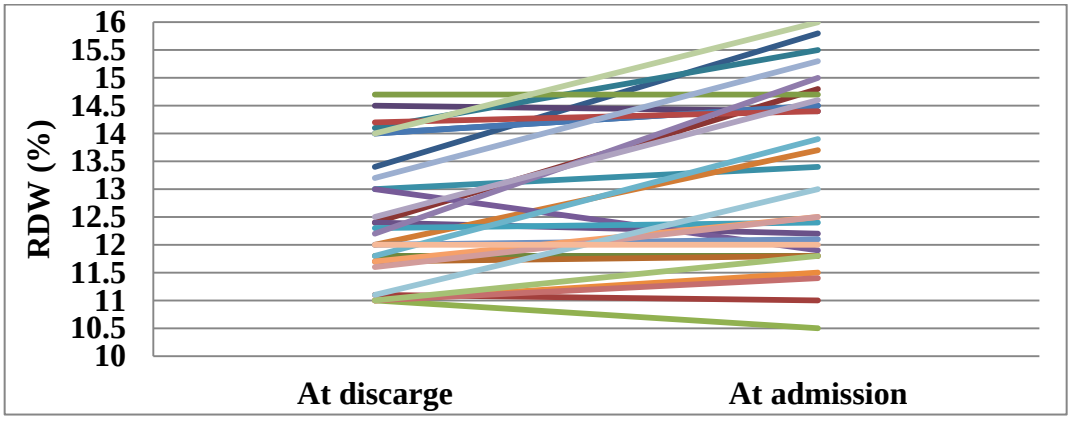

Figure 4: Comparison between cases at the time of admission and discharge in RDW.

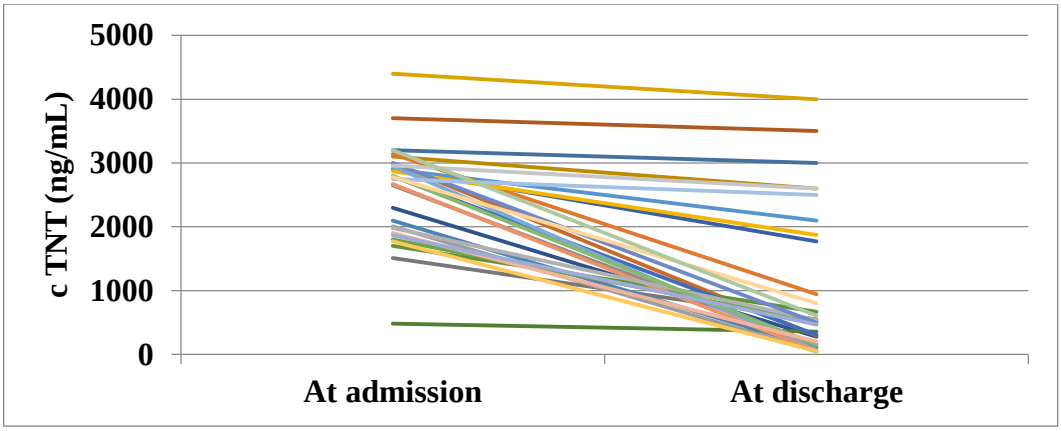

Figure 5: Comparison between cases at the time of admission and discharge in cTNT.

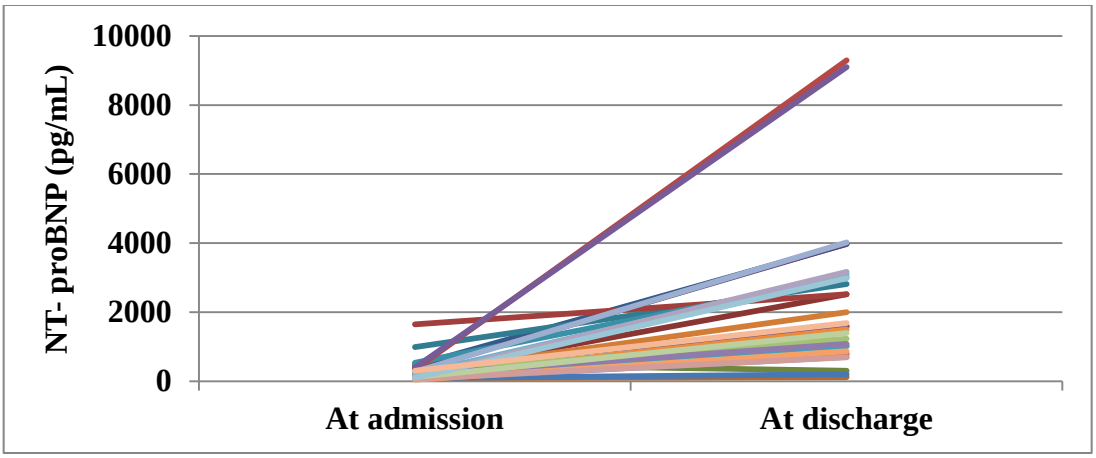

Figure 6: Comparison between cases at admission and discharge in NT- proBNP

There was a significant positive correlation between RDW assessment at discharge with either cTnT or NT-proBNP assessment at discharge (P-value < 0.05), as described in Table (4) and Figures (7) and (8).

Table 4: Correlation between (RDW) with (cTnT) and (NT-proBNP) of AMI cases.

	RDW (%)	
	r value	**P-value** ^^
At admission		
cTnT (ng/mL)	0.3	0.06
NT-proBNP (pg/mL)	0.2	0.3
At discharge		
cTnT (ng/mL)	0.4	0.02*
NT-proBNP (pg/mL)	0.4	0.02*

* Level of significance < 0.05, ^^ P-value is calculated by Spearman's correlation

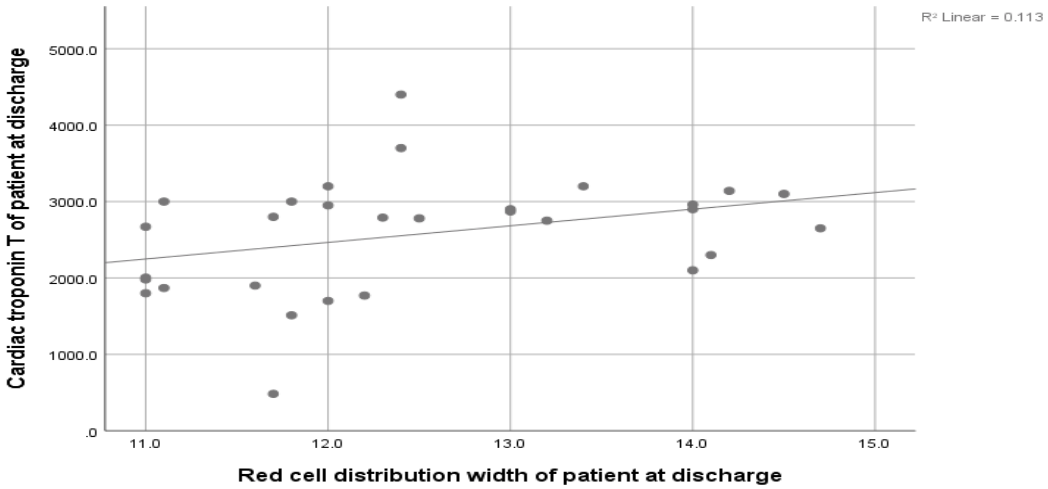

Figure 7: Correlation between RDW with cTnT at discharge of AMI cases.

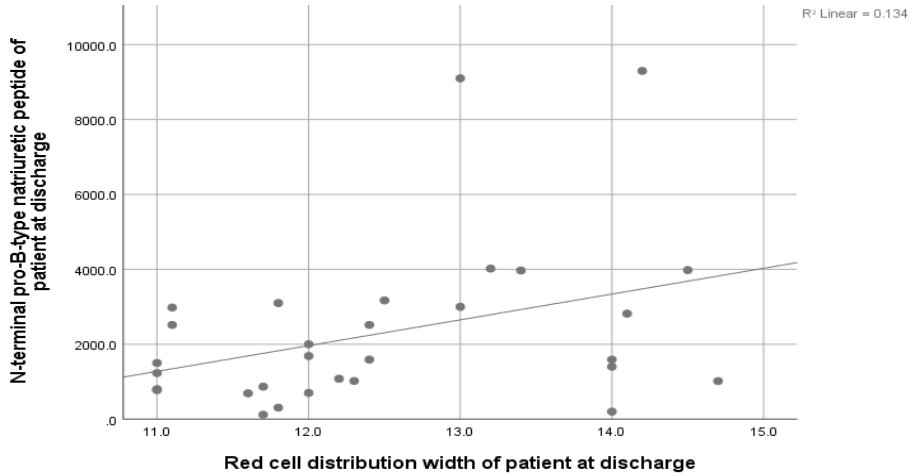

Figure 8: correlation between RDW with NT-proBNP at discharge of AMI cases.

There was a significant positive correlation between cTnT with NT-proBNP either at admission or at discharge (P-value < 0.05), as shown in Table (5) and Figures (9) and (10).

Table 5: Correlation between (cTnT) with (NT-proBNP) of AMI cases.

	cTnT (ng/mL)	
	r value	**P-value^^**
At admission		
NT-proBNP (pg/mL)	**0.4**	**0.02***
At discharge		
NT-proBNP (pg/mL)	**0.5**	**0.01***

* Level of significance < 0.05, ^^ P-value is calculated by Spearman's correlation

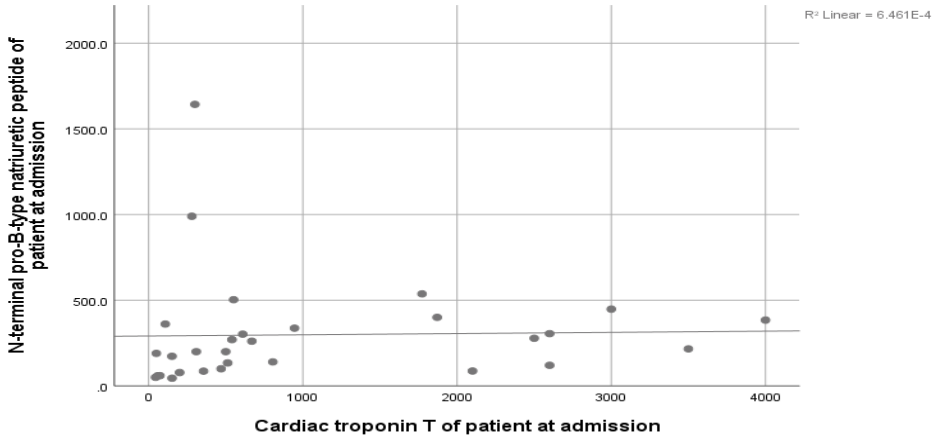

Figure 9: Correlation between cTnT with NT-proBNP at admission of AMI cases.

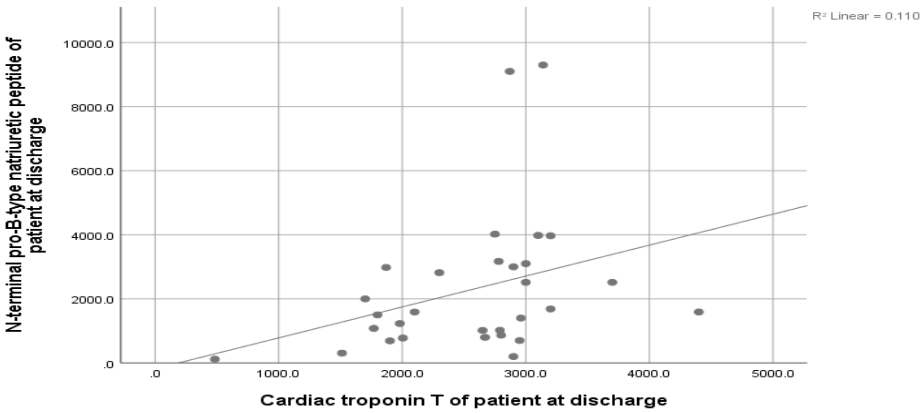

Figure 10: Correlation between cTnT with NT-proBNP at discharge of AMI cases.

Discussion

People should be prepared for the possibility that acute myocardial infarction (AMI) may become a global pandemic. Because it is the rapid loss of heart tissue caused by severe and chronic ischemia, it is the main killer. Medications for statins, catheter-based reperfusion, fibrinolytic therapy, and Acute myocardial infarction have seen a precipitous drop in both incidence and fatality rates over the last 30 years, with the help of coronary care units. The acute coronary syndrome describes this medical emergency. The future consequences of atherosclerotic coronary artery disease will be worsened by an aging population in developed nations and a worldwide rise in the prevalence of diabetes and obesity [(11)].

Ischemia symptoms, alterations in the ECG, and increased circulating cardiac biomarkers are the diagnostic tools used to diagnose AMI in acutely ill individuals. Heart troponins (cTns) are a "gold standard" for diagnosing AMI in its early stages because of how well they identify heart injury and how sensitive they are.

If a patient has acute coronary syndrome, NT-proBNP may predict their risk of death, acute heart failure, and atrial fibrillation (AF) development. [(12)].

One numerical measure for the variety in circulating erythrocyte size is the red blood cell distribution width (RDW). The RDW, or red cell distribution width, is a biological marker for cardiovascular illness. It is the proportion of erythrocyte volume fluctuation. In this population of patients, higher levels may represent a risk factor for worse clinical outcomes. [(13)].

We set out to compare a healthy control group with patients suffering from acute myocardial infarction (AMI) and see how several CBC parameters-including RDW, N-terminal NT-proBNP, and cardiac troponin T (cTnT)-correlated with one another. Thirty patients with AMI and fifteen healthy controls were the subjects of a case-control study that ran from March 1, 2023, to September 30, 2023.

The present research showed that about the cTnT level in the participants, there was a notable rise in cases at discharge compared to admission and the control group (2572.6 ± 755.6, 1054.3 ± 1007.4 and 27.7 ± 6.6) (ng/mL) correspondingly.

That lines up with what researchers found in May 2011 and May 2012 at China's Sun Yat-Sen University's First Affiliated Hospital in Guangzhou. The study included 56 individuals who had experienced an acute myocardial infarction (AMI) and 28 healthy individuals who had never had an AMI before. The purpose of this study was to determine the diagnostic utility of circulating miR-1 and cardiac troponin T (cTnT) in the early diagnosis of acute myocardial infarction (AMI) by measuring the levels of both in patients. Its secondary objective was to examine miR-1's biomarker potential for this early diagnosis. At admission, AMI patients' average cTnT levels were 1.35±1.10 ng/mL, which was

substantially higher than the control group's levels ($P < 0.01$), according to the data analysis. [14].

A 2015 research that evaluated cTnT concentrations at admission and discharge to predict significant cardiovascular events both during hospitalization and at six months of follow-up is consistent with our results. Results showed that 74% of patients with AMI were cTnT positive upon admission, 26% were cTnT negative at admission, and 35% of patients with positive results had serum cTnT levels that were higher upon discharge from the cardiac intensive care unit (CCU) than their admission or 24-hour levels..[15].

The findings indicated that the proportion of RDW was significantly higher for cases at admission (13.2 ± 1.5), discharge (12.4 ± 1.1), and control group (12.1 ± 0.8) percent, respectively.

Researchers in Verona, Italy, set out in 2009 to see if patients complaining of chest discomfort had a higher chance of having a correlated RDW at admission and an elevated cardiac troponin T (cTnT). The median RDW was 15.1% and the p-value was less than 0.001 among the 2304 adult patients who had ACS out of the total 2304 patients. The patients' complaints of chest pain were indicative of ACS. [16]

About NT-proBNP, the present research found that there was a notable rise in instances at discharge compared to admission and the control group (2301 ± 2199.2, 298.5 ± 321, and 44.6 ± 8.4) (pg/mL, respectively).

The AMI group had significantly higher NT-proBNP levels (943 vs. 162.5 pg/ml, p = 0,0001) compared to electrocardiography, transthoracic echocardiography, and coronary angiography. according to research that compared 66 patients hospitalized with AMI to healthy controls. [17].

According to RDW, cTnT, and NT-proBNP, there was a significantly significant difference between cases at admission and discharge (P-value < 0.05). When comparing RDW at admission (12.4 ± 1.1) with RDW at discharge (13.2 ± 1.5) across cases, there is a notable reduction in the mean of RDW. On the other hand, compared to the level at admission (2572.6 ± 755.6) and discharge (2574.3 ± 1158.4), the cTnT of cases significantly increases. In comparison to the levels at admission (2301 ± 2199.2 and 298.5 ± 321), NT-proBNP also exhibits a notable rise at discharge.

This result is in line with a study that aimed to investigate the relationship when it came to 2015 AMI patients' RDW and the deformability of their erythrocytes. A total of 62 patients with AMI and 72 healthy controls were matched according to age and gender in the experiment. Compared to the control group, patients had a significantly higher RDW (p = 0.012). [18].

We found different results from a retrospective research that included 101 patients with AMI and was carried out at Hunan Provincial People's Hospital in Changsha, China. Serum NT-proBNP, cTnI, MLR, NLR, and RDW-CV were all found to be significantly higher in AMI patients on the day of admission compared to either the day before or the day of discharge, according to CBC results [19].

The connection between RDW, cTnT, and NT-proBNP was rather favorable when evaluating RDW at discharge concerning either cTnT or NT-proBNP at discharge (P-value < 0.05). Statistical significance was not achieved, despite a link between RDW and cTnT at admission (r = 0.03, P-value = 0.06).

This contradicts the results of a study conducted in 2015 in Bursa, Turkey, which included 251 people who were brought to the critical care unit sequentially with non-ST-elevation acute coronary syndrome. The purpose of this study was to determine if there was a corr elation between the participants' red blood cell dispersion width measures and their cardiac troponin I levels. Results showed that RDW was able to foretell that individuals with NSTE-ACS will have more myocardial damage. Patients with NSTE-ACS had elevated cTnI levels, which were shown to be significantly related to RDW, indicating that RDW may be used as an extra metric for assessing these patients (P-value <0.05). [20].

Our findings differed because we used data acquired from 20,78 patients at the First Affiliated Hospital of Nanjing Medical University in China in 2015 and 2016. People who complained of

chest pain were considered to have had an acute myocardial infarction (AMI). No correlation was found between RDW and myocardial injury risk, however cTnT was (r=0.607). [21]

In contrast to the findings of Shen et al., we failed to find any evidence of a correlation between RDW and RDW-CV, blood NT-proBNP, and cTnI levels upon admission or on the day before or after discharge. We were unable to make any definitive findings on a link between RDW and cTnT due to our inadequate data.

Based on the relationship between the two variables (P-value < 0.05), we found a somewhat positive correlation between cTnT and NT-proBNP at admission and discharge.

In addition, our findings were in line with a study that examined 40 patients admitted to the emergency departments of Ain Shams University and Misr University for Sciences and Technology (MUST) Hospitals between 2021 and 2022 for STEMI and primary PCI revascularization. In patients who re-emerged with STEMI after primary PCI, the goal of the research was to find out whether the pre-PCI NT-pro BNP level could be utilized to predict successful reperfusion. Factors including symptom duration, contrast dose, total procedure time, HS Troponin levels, and EF were shown to have a substantial association with the pre-and post-operation NT-pro BNP level (r = 0.39, P-value = 0.012). [22]

There was a slight correlation between NT-proBNP concentrations and levels of hsTnT at randomization (r = 0.38, p < 0.001) in a study that looked at 1129 patients who had an acute myocardial infarction (AMI) and had either left ventricular systolic dysfunction, pulmonary congestion, or both [23]

Conclusion

AMI is the major cause of death worldwide; thus, the requirement for early diagnosis is becoming increasingly important to allow initiation of lifest-yle changes or appropriate medical intervention.

High levels of RDW were associated with AMI at admission and RDW is a widely available marker with no additional costs, in contrast to other novel markers of cardiovascular risk.

A high RDW may be associated with the severity and instability of acute myocardial infarction.

The combined use of presentation values of cTnT and its absolute change in the following hours has a significantly higher diagnostic accuracy for AMI than relative changes and seems therefore to be the preferred criteria to distinguish AMI from other causes of cTn elevations.

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